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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/463,494	07/25/2000	MANFRED T. REETZ	STUDIEN-268-	6396

7590

04/02/2004

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NEW YORK, NY 10017

EXAMINER
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PATTERSON, CHARLES L JR

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 04/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/463,494

**Applicant(s)**

REETZ ET AL.

**Examiner**

Charles L. Patterson, Jr.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 08 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 42-47 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 42-47 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 07 January 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

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A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/8/04 has been entered.

Applicants state that the examiner indicated in his last action that that there was an objection to the drawings and that "[f]ormal drawings were filed on September 8, 2003". There were formal drawing filed 1/7/03 and these drawings are approved.

Claims 42 and 45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims are indefinite in the recitation of "testing and identifying a mutant hydrolase having improved stereoselectivity or regioselectivity properties" in steps d) or e), respectively. The step now is drawn to identifying any mutant hydrolase when what was apparently intended was identifying the mutant hydrolase of the previous step for improved stereoselectivity or regioselectivity properties. Changing "a mutant hydrolase" to "said mutant hydrolase" would overcome the instant rejection.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at

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the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 42-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over either of Nakanishi, et al. (N), Hirose, et al. (U-2) or Krainev, et al. (V-2) in view of Williams, et al. (A), Zhou, et al. (U), Leung, et al. (V), Cadwell, et al. (W), Shinkai, et al. (X), Stemmer (V-1) and Zhang, et al. (W-1).

Nakanishi, et al. teach a method for modifying the stereoselectivity of an lipase by mutating one or several amino acids. Hirose, et al. teach that mutagenesis can be used to change to stereospecificity or stereoselectivity of lipases and states in the last sentence that "the present study gives an important suggestion to the origin of stereospecificity of a lipase". Krainev, et al. teach that mutations can produce enzymes with altered chiral discrimination for binding R, S, + and - compounds. This is binding is "improved stereoselective or regioselective properties", as in the instant claims. All of these references use site directed mutagenesis.

The seven secondary references each teach a method of random mutagenesis to study what effect it has on a protein. In Williams, et al, column 1, lines 11-23 it is stated that while "site-directed mutagenesis...typically requires information on the structure-function relationship of the protein under study...random mutagenesis of the DNA region of interest coupled with adequate screening or selection procedures provides an alternative and general method for the generation of DNA, RNA or protein species with improved or novel functions in the absence of initial structural information". Leung, et al. state in the first paragraph in column 1 of page 11 that "[r]andom mutagenesis of the DNA region of interest coupled to a screening system is there-

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fore generally the method of choice for the study of a gene or its regulatory functions". Cadwell, et al. state in the first paragraph in the middle column on page 28 that [r]andom mutagenesis coupled with a screening method, is especially useful when functionally significant positions are not well known". In the first full paragraph on page 4508 of Zhang, et al. it is stated that "[o]ne major advantage of *in vitro* evolution [which the method of the reference is called] of enzymes over the structural modeling is that only minimal information is required for improving the desired phenotype".

It would have been obvious to one of ordinary skill in the art to combine the teachings of the primary references that mutagenesis can be used to change the stereoselectivity of enzymes along with the teachings of the secondary references that there are various methods of random mutagenesis that may be used and that in general the random mutagenesis methods require less information about the protein than other methods such as site-directed mutagenesis, to mutate enzymes by one or more of the random mutagenesis method taught by the secondary references. It would have been further obvious to test the mutated enzyme to see if had improved stereoselectivity and/or regioselectivity. Although Krainev, et al. teaches mutagenesis of a cytochrome P45, which is defined in the introduction as being a monooxygenase, it is maintained that the method would have been obvious to study the stereospecificity of all enzymes. The motivation would have been to study the stereoselectivity and/or regioselectivity of enzymes when not much is known about the structure-function relationships of the enzyme.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charles L. Patterson, Jr., PhD, whose telephone number is 571-272-0936. The examiner can normally be reached on Monday - Friday from 7:30 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-308-4242.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Charles L. Patterson, Jr.  
Primary Examiner  
Art Unit 1652

Patterson  
March 30, 2004